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IFW

CASE PA-4-32473A



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April 11, 2005
Date of Deposit

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE PCT NATIONAL STAGE APPLICATION OF
BEERLI ET AL.

INTERNATIONAL APPLICATION NO: PCT/EP03/04433

FILED: 28 APRIL 2003

U.S. APPLICATION NO: 10/509,316

35 USC §371 DATE: 27 SEPTEMBER 2004

FOR: CRYSTAL STRUCTURE OF THE LIGAND BINDING DOMAIN OF
THE RETINOIC ACID-RELATED ORPHAN RECEPTOR ALPHA
(ROR-ALPHA)

MS: Amendment

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Sir:

Applicants believe this paper is being filed before the mailing date of a first Office action on the merits, and so under 37 C.F.R. §1.97(b)(3) no fees are required. If a fee is deemed to be required, the Commissioner is hereby authorized to charge such fee to Deposit Account No. 19-0134.

In accordance with 37 C.F.R. §1.56, applicants wish to call the Examiner's attention to the references cited on the attached form(s) PTO-1449.

The asterisked references were cited in the International Search Report and since copies of said references were forwarded by the International Bureau, only copies of the non-asterisked references are enclosed.

The Examiner is requested to consider the foregoing information in relation to this application and indicate that each reference was considered by returning a copy of the initialed PTO 1449 form(s).

Respectfully submitted,

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Attorney for Applicants
Reg. No. 46,280

Enclosures: PTO-1449 and references

Date: April 11, 2005

INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

ATTY. DOCKET NO.

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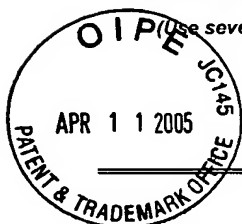
APPLICANT

BEERLI ET AL.

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U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE
	AA						
	AB						
	AC						
	AD						
	AE						
	AF						
	AG						
	AH						
	AI						
	AJ						
	AK						
	AL						

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	OFFICE	CLASS	SUBCLASS	TRANSLATION	
							YES	NO
	AM	WO 03/000732 A2	1/3/03	PCT			<input type="checkbox"/>	<input type="checkbox"/>
	AN	WO 01/26737 A2	4/19/01	PCT			<input type="checkbox"/>	<input type="checkbox"/>
	AO	WO 99/50660	10/7/99	PCT			<input type="checkbox"/>	<input type="checkbox"/>
	AP	WO 95/27202	10/12/95	PCT			<input type="checkbox"/>	<input type="checkbox"/>
	AQ						<input type="checkbox"/>	<input type="checkbox"/>

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent pages, Etc.)

	AR	Acta Cryst., "The CCP4 Suite: Programs for Protein Crystallography", D50, pp. 760-763, (1994).
	AS	Atkins, et al., "Coactivators for the Orphan Nuclear Receptor RORa", Molecular Endocrinology, Vol. 13, No. 9, pp. 1550-1557, (1999).
	AT	Becker-Andre, et al., "Identification of Nuclear Receptor mRNAs by RT-PCR Amplification of Conserved Zinc-Finger Motif Sequences", Biochemical and Biophysical Research Communications, Vol. 194, No. 3, pp. 1371-1379 (1993).

EXAMINER

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*EXAMINER: Initial of reference considered, whether or not citation is in conformance with MPEP 609: Draw a line through citation if not in conformance and not considered. Include a copy of this form with the next communication to applicant.

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DA	Bernstein, et al., "Probing the Limits of the Molecular Replacement Method: the Case of Trypanosoma Brucei Phosphoglycerate Kinase", Acta Cryst, D53, pp. 756-764, (1997).
DB	Blessing, et al., "Difference Structure-Factor Normalization for Heavy-Atom or Anomalous-Scattering Substructure Determinations", J. Appl. Cryst., 32, pp. 664-670, (1999).
DC	Bordji, et al., "Evidence for the Presence of Peroxisome Proliferator-Activated Receptor (PPAR) α and γ and Retinoid Z Receptor in Cartilage", The Journal of Biological Chemistry, Vol. 275, No. 16, pp. 12243-12250, (2000).
DD	Brown, et al., "The SREBP Pathway: Regulation of Cholesterol Metabolism by Proteolysis of a Membrane-Bound Transcription Factor", Cell, Vol. 89, pp. 331-340, (1997).
DE	Brunger, et al., "Crystallography & NMR System: A New Software Suite for Macromolecular Structure Determination", Acta Cryst., D 54, pp. 905-921, (1998).
DF	Cleverley, et al., "Characterization of Cholesterol-Free Insect Cells Infectible by Baculoviruses: Effects of Cholesterol on VSV Fusion and Infectivity and on Cytotoxicity Induced by Influenza M2 Protein", Experimental Cell Research, 233, pp. 288-296, Article No EX973573 (1997)
DG	De La Fortelle, et al., "Maximum-Likelihood Heavy-Atom Parameter Refinement for Multiple Isomorphous Replacement and Multiwavelength Anomalous Diffraction Methods", Methods in Enzymology, Volume 276, pp. 472-494.
DH	Delerive, et al., "The Orphan Nuclear Receptor ROR α is a Negative Regulator of the Inflammatory Response", EMBO Reports, Vol. 2, No. 1, pp. 42-48, (2001).
DI	Dunbrack, Jr., et al., "Meeting Review: the Second Meeting on the Critical Assessment of Techniques for Protein Structure Prediction (CASP2), Asilomar, California, December 13-16, 1996", Folding & Design, Vol. 2, No. 2, pp. R27-R42, (1996).
DJ	Engh, et al., "Accurate Bond and Angle Parameters for X-Ray Protein Structure Refinement", Acta Cryst., A47, pp. 392-400, (1991).
DK	Geiser, et al., "Integration of PCR Fragments at Any Specific Site Within Cloning Vectors without the Use of Restriction Enzymes and DNA Ligase", BioTechniques, Vol. 311, No. 1, Short Technical Reports, (2001).
DL	Giguere, et al., "Isoform-Specific Amino-Terminal Domains Dictate DNA-Binding Properties of ROR α , a Novel Family of Orphan Hormone Nuclear Receptors", Genes & Development, 8:538-553, (1994).
DM	Goldstein, et al., "Receptor-Mediated Endocytosis of Low-Density Lipoprotein in Cultured Cells", Methods in Enzymology, Vol. 98, Part L, pp. 241-260, (1983).
DN	Jones, et al., "Improved Methods for Building Protein Models in Electron Density Maps and the Location of Errors in these Models", Acta Cryst., A47, pp. 110-119, (1991).

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	DA	Kallen, et al., "X-Ray Structure of the hRORa LBD at 1.63 Å: Structural and Functional Data that Cholesterol or a Cholesterol Derivative is the Natural Ligand of RORa", Structure, Vol. 10, pp. 1697-1707, December, (2002).*
	DB	Kleywegt, et al., "Dictionaries for Heteros", News from the Uppsala Software Factory - 5, pp. 45-50.
	DC	Laskowski, et al., "Computer Programs", J. Appl. Cryst. 26, pp. 283-291, (1992).
	DD	Moraitis, et al., "Transition from Monomeric to Homodimeric DNA Binding by Nuclear Receptors: Identification of RevErbAa Determinants Required for RORa Homodimer Complex Formation", Molecular Endocrinology, pp. 431-439, (1999).
	DE	Nolte, et al., "Ligand Binding and Co-Activator Assembly of the Peroxisome Proliferator-Activated Receptor-γ", Nature, Vol. 395, pp. 137-143, (1998).
	DF	Nwokoro, et al., "Genetic Disorders of Cholesterol Biosynthesis in Mice and Humans", Molecular Genetics and Metabolism, 74, pp. 105-119, (2001)
	DG	Otwinowski, et al., "Processing of X-Ray Diffraction Data Collected in Oscillation Mode", Methods in Enzymology, Vol. 276, pp. 307-326 (1997)
	DH	Pittenger, et al., "Multilineage Potential of Adult Human Mesenchymal Stem Cells", Science, Vol. 284, April (1999)
	DI	Renaud, et al., "Crystal Structure of the RAR-γ Ligand-Binding Domain Bound to All-Trans Retinoic Acid", Nature, Vol. 378, (1995)
	DJ	Renaud, et al., "Structural Studies on Nuclear Receptors", CMLS Cellular and Molecular Life Sciences, 57, pp. 1748-1769, (2000)
	DK	Robyr, et al., "Nuclear Hormone Receptor Coregulators in Action: Diversity for Shared Tasks", Molecular Endocrinology, pp. 329-347, (2000)
	DL	Simons, et al., "Cholesterol Depletion Inhibits the Generation of B-Amyloid in Hippocampal Neurons", Proc. Natl. Acad. Sci. USA, Vol. 95, pp. 6460-6464, (1998)
	DM	Stehlin, et al., "X-Ray Structure of the Orphan Nuclear Receptor RORB Ligand-Binding Domain in the Active Conformation", The EMBO Journal, Vol. 20, No. 21, pp. 5822-5831 (2001)*
	DN	Stevens, "High-Throughput Protein Crystallization", Current Opinion in Structural Biology, 10, pp. 558-563 (2000)*

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DA	Stocco, "StAR Protein and the Regulation of Steroid Hormone Biosynthesis", Annu. Rev. Physiol., 63, pp. 193-213, (2001).
DB	Strittmatter, et al., "Apolipoprotein E: High-Avidity Binding to B-Amyloid and Increased Frequency of Type 4 Allele in Late-Onset Familial Alzheimer Disease", Proc. Natl. Acad. Sci. USA, Vol. 90, pp. 1977-1981, March (1993)
DC	Sundvold, et al., "Identification of a Novel Peroxisome Proliferator-Activated Receptor (PPAR) γ Promoter in Man and Transactivation by the Nuclear Receptor ROR α 1", Biochemical and Biophysical Res. Comm., 287, pp. 383-390 (2001)
DD	Vagin, et al., "MOLREP: An Automated Program for Molecular Replacement", J. Appl. Cryst., 30, pp. 1022-1025, (1997)
DE	Villasenor, et al., "Fast Drops: A High-Throughput Approach for Setting Up Protein Crystal Screens", BioTechniques, 32, pp. 184-189, (January, 2002)*
DF	Weeks, et al., "The Design and Implementation of SnB Version 2.0", J. Appl. Cryst., Computer Programs, 32, pp. 120-124, (1999)
DG	Wurtz, et al., "A Canonical Structure for the Ligand-Binding Domain of Nuclear Receptors", Nature Structural Biology, Vol. 3, No. 2, (February 1996) (1 page)
DH	Wronski, et al., "Long-Term Effects of Ovariectomy and Aging on the Rat Skeleton", Calcified Tissue International, 45, pp. 360-366, (1989)
DI	PCT International Search Report based on PCT/EP03/04433; International Filing Date: April 28, 2003 along with cover pages (9 pages)
DJ	McBroom et al., 1995, Mol. Cell. Biol. 15:796-808.
DK	
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